## XIII.

## **National Institute on Drug Abuse**

#### INTRODUCTION

It is the mission of the National Institute on Drug Abuse (NIDA) to lead the Nation in bringing the power of science to bear on drug abuse and addiction. The two critical components of this charge are (1) the strategic support and conduct of research across a broad range of disciplines and (2) the rapid and effective dissemination and application of the results of that research to significantly improve prevention, treatment, and policy in relation to drug abuse and addiction.

The international program implements the NIDA mission through coordination with international and regional organizations, with other agencies of the U.S. Government, and with nongovernmental organizations involved in research on drug abuse and related health consequences. Through the International Visiting Scientists and Technical Exchange (INVEST), NIDA fosters international research collaboration through technical consultation, scientific exchange, information dissemination and international communications networks, and research fellowships.

#### HIGHLIGHTS OF RECENT SCIENTIFIC ADVANCES RESULTING FROM INTERNATIONAL ACTIVITIES Canada

#### Long-term Use of Methamphetamine

A NIDA-supported researcher at Clarke Institute of Psychiatry, Toronto, Ontario, is focused on identifying changes in the brain of long-term users of methamphetamine, as well as other drugs that might be responsible for the behavioral and possible neurotoxic consequences of long-term drug exposure. In preclinical studies, the principal investigator explored the mechanisms of methamphetamine neurotoxicity. He examined binge use of methamphetamine versus long-term, daily administration and found that bingeing was associated with a

regionally specific reduction of glutathione, an antioxidant that protects neural cells from oxidative stress, which can lead to neurotoxicity. This finding suggests that medications designed to increase glutathione might protect against oxidative damage brought about by drugs of abuse.

In a clinical study in fiscal year 1999 (FY 99), the researcher measured the activity of choline acetyltransferase, a marker enzyme for cholinergic brain cells, in brains obtained at autopsy of long-term users of one or more of the drugs cocaine, methamphetamine, and heroin. His studies revealed that 2 of 12 methamphetamine users, who had the highest brain-blood drug levels at autopsy, had a severe depletion (up to 94%) of this enzyme in different brain regions (cerebral cortex, striatum, and thalamus). He reported that the neurochemical data suggest that damage to cholinergic brain neurons is not typical for long-term use of cocaine, methamphetamine, or heroin, but that exposure to very high doses of methamphetamine could damage this neuronal system and lead to impairments of cognitive function.

## Prenatal Exposure to Cannabis and Tobacco

A study on Prenatal Cannabis and Cigarette Exposure—Outcomes in Adolescents and Young Adults, with Carleton University, Ottawa, Ontario, was in the 12th year of a 15year project in FY 99. One of only two such cohort studies in the United States and Canada, this critical project examines health and development outcomes after prenatal exposure to marijuana. The children in this sample, with follow-up since birth, are now 16½-19½ years old. Consequently, this research affords immense opportunity to acquire previously unattainable information, including new knowledge on initiation and patterns of drug use for adolescents and young adults who were exposed to illicit drugs in utero.

Specific observations for children 9–12

years old include the finding that maternal use of marijuana during pregnancy is associated with markedly different child outcomes than is maternal use of tobacco during pregnancy. Childhood outcomes of prenatal exposure to marijuana appear to be consistent with findings in the literature on outcomes in adult, nonpregnant, longterm users of marijuana and on the neurophysiological effects of marijuana in animals. These effects in animals relate to the distribution of cannabinoids and cannabinoid receptors in the nervous system, which implicates the frontal region of the brain. Furthermore, together with observations made when the children were younger, results at 9-12 years of age suggest that prenatal marijuana exposure may influence specific aspects of executive function. Preliminary findings for children 13½–16 years old also indicate a clear association of prenatal marijuana with later executive function, rather than with more general measures of cognition such as IQ (intelligence quotient). In contrast, the effects of maternal cigarette use during pregnancy seem to relate to behaviors involving auditory processing and measures of general intelligence in children. The researchers are continuing to study these differential outcomes.

#### **G Protein-Coupled Receptors**

A NIDA-supported investigator and his colleagues at the University of Toronto were the first to provide evidence that G protein—coupled receptors (GPCRs) exist as dimers; this finding opened a new area of active research. They also were among the first to report the polymorphic variation of dopamine receptors in human subjects (a repeat of 48 base pairs in the DNA of D4 dopamine receptors). Among their significant advances were findings about receptor function and genes and behavior.

#### Receptor Function

The investigators established that the high-

er-molecular-weight species observed for all the GPCRs they studied (e.g., D<sub>1</sub> and D<sub>2</sub> dopamine receptors and serotonin 5HTlB receptors) are receptor oligomers. They provided evidence for the universality of oligomerization in the GPCR family. D<sub>2</sub> dopamine receptor dimers and tetramers were documented in cultured cells and in the human brain, and D2 dopamine receptors were found to exist as oligomers in the cell. Using photoaffinity labeling, the investigators provided the first indication that different classes of dopamine antagonists may have differential affinity for receptor monomers and dimers. Different antipsychotic drugs were found to bind loosely to D<sub>2</sub> dopamine receptors, but they retained high occupancy. Agonist activation of D<sub>2</sub> dopamine receptors resulted in an increase of monomers and dimers on the cell surface. The ability of closely related receptors to heterodimerize was examined by using the serotonin 5HTlB and 5HTlD receptors, which clearly showed a preferential ability to heterodimerize rather than to homodimerize. The investigators also examined the ability of the  $\mu$  and  $\delta$  opioid receptors to interact at the level of the receptors and demonstrated evidence for a novel and unique pharmacology. They tested the hypothesis that peptides based on the transmembrane domains of GPCRs could act as antagonists of the receptor from which they were derived. With use of the D<sub>1</sub> dopamine receptor as a model, a synthetic peptide derived from transmembrane 6 of the receptor was shown to inhibit antagonist binding. The peptide also inhibited agonist-independent and agonist-dependent G protein binding and adenylyl cyclase activation. Thus the investigators showed, for the first time, that a peptide with the amino acid sequence of the hydrophobic transmembrane domain of the D<sub>1</sub> dopamine receptor had a specific antagonistic effect on its function. They extended these findings with other GPCRs to demonstrate that this strategy has potential for selective receptor antagonism.

#### Genes and Behavior

These investigators established a breeding colony of knockout mice in which the function for the D1 dopamine receptor was neutralized. The colony consists of three populations—wild-type, heterozygous, and homozygous animals, confirmed by DNA

genotyping. The researchers showed that perception of reward was abolished in D<sub>I</sub>-/D<sub>I</sub>-mice and that preference for alcohol was markedly reduced. These animals also demonstrated a marked reduction of spatial learning and of response to substances of abuse.

#### China

Researchers from Beijing Medical University continued to report their findings about the physiological basis of acupuncture analgesia. During FY 99, the principal investigator found that the κ opioid agonist U50488H suppressed calcium currents in the dorsal root ganglion. This effect was almost completely reversed by the antiopioid peptide orphanin FQ. In a related study, nocistatin blocked the antagonism of morphine analgesia produced by orphanin FQ in the rat. These studies contribute to better understanding of the function of orphanin FQ in pain processing. The investigator also compared rats that were very responsive to electroacupuncture with rats for which this procedure did not produce analgesia. The rats that did not show analgesia after electroacupuncture had higher levels of cholecystokinin 8 (CCK-8) in the spinal cord. This finding suggests that spinal levels of CCK may be inversely related to the response of rats to electroacupuncture. In a further series of studies, the investigator examined the levels of electroacupuncture that induce the release of somatostatin and calcitonin gene-related peptide, two neuropeptides involved in pain processing.

#### Colombia

A prospective longitudinal study of Colombian youth who were adolescents at study entry and their parents was in its 4th year in FY 99. Researchers at Mt. Sinai School of Medicine, New York City, New York, and Universidad de Antioquia, Medellín, are examining the causes of patterns and changes in adolescent drug use, other problem behaviors, and the consequences of drug use on the individual and the family. Findings published in FY 99 support a family interactional theory. Factors related to family traits and adolescent personality, as well as peer factors, had a direct effect on adolescents' marijuana use. Gender-specific differences in the influence of the cultural and ecological domain on drug use were observed. Among adolescent boys, the effects of this domain were indirect (i.e., mediated by family, peer, and personality factors). A direct effect of the cultural and ecological domain was detected among adolescent girls, in addition to the indirect cultural and ecological effect on marijuana use observed among boys. The developmental path leading to drug use among Colombian adolescents does not appear to differ markedly from the path that has been found among white, African-American, and Puerto Rican adolescents living in the United States. Nevertheless, there were marked cultural differences, which were reflected in genderspecific differences in the pathways to marijuana use. Both familism and religion, two important cultural values, were more likely to protect the adolescent from drug use in Colombia than in the United States. Another report from this team of researchers indicates that sensation seeking and tolerance of deviance were similarly related to both delinquency and marijuana use, suggesting that a common cause underlies the propensity to engage in different deviant behaviors. When violence is endemic and illicit drugs are readily available, a close parent-child bond was capable of mitigating these risk factors, leading to less marijuana use and delinquency.

#### Croatia

A scientist from Ruder Boskovic Institute. Zagreb, was trained in opioid immunopharmacology with support from a NIDA INVEST fellowship. The scientist reported that κ opioid receptors are expressed on mouse lymphocytes and on modified cell lines. The purpose of the investigation is to study the regulation of calcium by opioids to determine whether the  $\kappa$  opioid receptor on cells of thymoma cell lines downregulates calcium and desensitizes when the cells are cultured in the presence of a k opioid agonist. She studied the effects of the synthetic к opioid U50488 on calcium transport into these mouse thymoma cells, which selectively express the κ opioid class of receptors. Calcium transport into these cells was not affected by the κ opioid agonist U50488 alone or in the presence of the plant lectins, phytohemagglutinin and concanavalin A, which are used to stimulate red blood cells. These findings were published in the International Journal of Immunopharmacology in

FY 99.The studies reported here are a part of the overall effort of this laboratory to clarify the role of opioids in immune function. This scientist will now be able to continue her research in Croatia with a better understanding and clarity of the function of opiates in disease processes such as acquired immunodeficiency syndrome (AIDS).

#### **New Zealand**

A collaboration has been forged between a researcher at Virginia Commonwealth University, Richmond, and the Christchurch School of Medicine to study twin pairs concordant for nicotine dependence. As the search for genes underlying complex diseases such as nicotine dependence and other drug addiction disorders continues, international research efforts are becoming increasingly important for two reasons: (1) Large numbers of subjects are required to determine the small effects of multiple genes on the disease under study. (2) Because individuals with different ethnic backgrounds have different genotypes, many genotypic variations contributing to a disease pattern need to be understood. This joint study has resulted in the discovery of several genes that are now receiving closer scrutiny as possible candidates underlying genetic risk for nicotine dependence.

#### **Sweden**

In FY 99, the University of Pennsylvania Treatment Research Center, Philadelphia, supported a series of laboratory studies at Karolinska Institute, Stockholm, which examined cell cultures from humans and rodents to identify changes in opioid peptide systems characteristic of opiate tolerance and dependence. The scientists hypothesized that these changes may be associated with increased risk for relapse to drug use in humans.

#### **Thailand**

Researchers at Johns Hopkins University, Baltimore, Maryland, working with Chang Mai University and the Northern Drug Dependence Treatment Center, Ministry of Public Health, Chiang Mai, are investigating the epidemiology of infection with human immunodeficiency virus (HIV) among persons who use opiates, amphetamines, or both types of drugs. The project, in its 2nd year in FY 99, is based in Chiang Mai. This

study is expected to determine risk factors for HIV infection and to ascertain the contribution of risk factors to acquisition of infection. Potential risk factors under study include drug injection practices, sexual behaviors, and history of sexually transmitted diseases. The researchers will also assess the prevalence and impact of other conditions that exacerbate the morbidity of HIV infection, such as tuberculosis and hepatitis, and will characterize HIV viral subtypes circulating among users of opiates, amphetamines, or both types of drugs. Analysis of data from the only inpatient drug treatment program in northern Thailand demonstrates high rates of new HIV infection, with the highest rates among opiate injectors, and more recent data indicate a growing problem with amphetamine use in this area.

In another collaboration between Johns Hopkins University and Chiang Mai University, investigators are studying the prevalence of hepatitis C among various populations, including drug users, commercial sex workers, patients with sexually transmitted diseases, and military recruits. The project, in its 1st year of funding in FY 99, will address the epidemiology and transmission of hepatitis C virus (HCV), as well as the virology and natural history of the disease in persons with or without HIV infection.

# SUMMARY OF INTERNATIONAL PROGRAMS AND ACTIVITIES Country-to-Country Activities and Bilateral Agreements

#### Australia

A NIDA-supported researcher from the University of Sydney is examining the effect of long-term administration of morphine on PAG neurons in mice. These pharmacologically and biophysically sophisticated studies may shed considerable light on the neuro-adaptations leading to drug dependence, allowing greater insight into the processes underlying addiction. This investigation is unique because it uses the combination of transgenic and neurophysiological approaches to dissect the mechanisms responsible for opioid tolerance and dependence.

#### Canada

During FY 99, an investigator at the University of Delaware, Newark, worked with investigators at the Center for Addiction and

Mental Health, Toronto, in the 1st year of a NIDA-funded extramural study to explore the linkage between drugs and violence among adolescents 14–17 years of age. The study is examining the experience and attitudes of adolescents in Philadelphia, Pennsylvania, and Toronto, to address the following questions:

- 1. Do drugs contribute to a significant amount of youth violence?
- 2. What are the patterns and correlates of drug-related violence among adolescents?
- 3. How do structural features of neighborhoods and other policy and environmental factors influence drug-related violence?
- 4. Can commonalities and differences identified in the two cities explain the relationship?

It is hoped that this study will increase understanding of the important issue of youth violence in contemporary society.

Under a NIDA grant, the University of British Columbia, Vancouver, is studying groups of adult injection drug users in Vancouver and in Montreal, Quebec, to determine trends in HIV seroincidence and to identify and explain why access to clean needles alone is not sufficient to halt HIV infection among injection drug users. Of particular interest is the impact that the type of drug, pattern of drug use, micro-social climate, macro-social climate, and attitudes have on HIV incidence in injection drug users. HIV-seropositive participants in the study are offered extensive pretest and posttest counseling and referrals for free medical and psychosocial care. In FY 99, analytic findings indicated that aboriginal people, a significant minority in Canada, were 1.6 times more likely than other injection drug users to have HIV seroconversion. This finding reflects the predilection for HIV infection in disadvantaged and minority populations in different countries and settings. Data also indicate that the HCV positivity rate is approximately 90% in the drug-injecting population. Among injection drug users, those who were HCV positive were more likely to be infected with HIV, more likely to have a history of incarceration, and more likely never to have been in a methadone treatment program than those who were HCV negative.

#### China

A joint study by researchers at Johns Hopkins University, Baltimore, the Guangxi Health and Anti-Epidemic Center, and the Chinese Academy of Preventive Medicine documented both prevalence and incidence of HIV infection and associated risk factors for infection among drug users. The study also will document the prevalence and distribution of HIV subtypes, determine the HIV subtypes in newly infected drug users, and compare the transmissibility of those subtypes among injection drug users and their sexual partners. The researchers will also track changes in risk profiles and viral subtypes over time.

#### **France**

NIDA funds a research grant to Institut National de la Santé et de la Recherche Médicale on the synthesis and evaluation of D<sub>3</sub> dopamine receptor ligands for treatment of cocaine abuse. The main goal of this project is to develop selective and partial D<sub>3</sub> dopamine agonists for use as treatment agents, in addition to BP 897, which is the partial and selective D<sub>3</sub> dopamine agonist developed by the principal investigator. During FY 99, the pharmacological testing of BP 897 was completed, and the results were published in Nature. In the in vivo studies, BP 897 showed no potential for abuse and reduced self-administration of cocaine in rats.

During FY 99, 73 new compounds were synthesized, and binding and function were evaluated. A strain of  $D_3$  dopamine knockout mice was bred, and *in vivo* studies were designed to provide important information on the role of the  $D_3$  dopamine receptor in drug abuse. In addition, methods were established for the pilot synthesis of BP 897, and a corporate partner has undertaken the toxicology and pharmacokinetic studies necessary for a phase I trial, which is planned for the near future.

#### Mexico

NIDA is funding researchers at the University of Texas, San Antonio, to conduct a cross-national study of sexual behavior that places injection drug users at risk for HIV, in two groups of U.S.-Mexico border cities: (1) El Paso, Texas, and Ciudad Juárez and Chihuahua, Mexico, and (2) Laredo, Texas, and Nuevo Laredo, Mexico. The purpose of the

study is to provide a greater understanding of the international implications of the epidemiology of HIV/AIDS. This study, which was in its 2nd year in FY 99, is designed to determine the nature and extent of injection drug use and high-risk sexual behavior along the U.S.-Mexico border. The study is using ethnographic and survey methods to gather data from injection drug users and commercial sex workers on both sides of the U.S.-Mexico border. Data on health and behavioral risk also will be collected from health system organizations, the criminal justice system, and social service agencies in the cities targeted by the study.

#### Russia

In FY 99, NIDA awarded an administrative supplement to the University of Pennsylvania Treatment Research Center, Philadelphia, to work with Russian psychiatrists at the Pavlov State Medical University, St. Petersburg, to assess the efficacy of naltrexone and sertraline, alone and in combination, plus manual-guided psychosocial treatment, to prevent relapse in heroin addicts receiving drug treatment, after detoxification, at a St. Petersburg medical facility where agonist pharmacotherapy is not available.

#### Sweden

FY 99 was the next to final year of a study being conducted at the Pharmacology Institute, Göteborg, to examine the behavioral sensitization to the combination of alcohol and nicotine in laboratory animals. The investigator found a cross-sensitization to nicotine and alcohol, as evidenced by the ability to activate the brain reward (mesolimbic dopamine) system. The researchers found that this effect is antagonized by a nicotine antagonist that does not work in the brain, suggesting that part of this crosssensitization involves peripheral receptors. The outcome of the study is important, because it may lead to a method of blocking the rewarding effects of nicotine or ethanol without interfering with higher brain functions such as cognition.

A NIDA-funded researcher at Karolinska Institute, Stockholm, initiated studies of the effects of cocaine on the normal development of the cerebral cortex, during FY 99. Taking advantage of important brain banks in both the United States and Sweden, the researcher is investigating expression of gene

function—both location in the brain and timing of developmental stages. Gene expression is an index of what, where, and when brain proteins are manufactured by neural cells. The hypothesis under study is how cocaine, specifically, and other substances, generally, affect changes in the normal development of brain circuitry. This research is important to understanding how drug taking by pregnant women affects the brain development of their offspring.

#### **Multicountry Projects**

In FY 99, a NIDA-funded investigator at Washington University, St. Louis, Missouri, was in the 3rd year of a study to analyze existing data from general population surveys that used comparable data collection instruments in Canada, New Zealand, South Korea, the United States, and Taiwan. The purpose of the analyses is to examine pathways from problems in childhood behavior and conduct to adult substance abuse. The investigator is exploring cross-societal differences in (1) associations between adult substance abuse and psychopathologic conditions and the severity, syndrome, and age at onset of conduct problems and (2) demographic cofactors and mediating or preceding psychopathologic conditions related to the onset of problems.

During FY 99, a researcher at the University of California, Santa Cruz, was in the 3rd year of a NIDA-funded extramural collaboration with independently funded researchers in Bremen, Germany, and Amsterdam, the Netherlands, to examine the course of marijuana use by persons in San Francisco, California, Bremen, and Amsterdam. The three studies are using comparable sampling strategies and data collection instruments. Results of comparative analyses are expected to contribute to understanding of the influence of psychological sets in marijuana users, social settings of use, and sociocultural variables and differences in legal policy on patterns of marijuana use, effects as a "gateway" to use of other drugs, dependence on drugs, and a range of other adverse health and social consequences.

A NIDA-funded investigator at Johns Hopkins University, Baltimore, worked for a 3rd year, in FY 99, in an extramural study with the Organization of American States Inter-American Drug Abuse Control Commission and investigators in Costa Rica, the Do-

minican Republic, El Salvador, Guatemala, Honduras, Nicaragua, and Panama to undertake a multisite cross-sectional, schoolbased survey of teenage drug involvement in these seven countries. The project includes the use of standardized classroom survey methods and will produce estimates of drug use by teenagers in each country, on the basis of a national probability sample survey. Results from the study will contribute to understanding of the characteristics of individuals, the conditions, and the processes that influence the occurrence of drug use, drug dependence, and other forms of serious drug involvement among youth.

In FY 99, a researcher at Harvard University, Boston, Massachusetts, was in the 4th year of a NIDA-funded extramural collaboration with researchers from several countries, to gather existing data sets from population-based surveys that used the Composite International Diagnostic Interview (CIDI). This effort is resulting in a unique multicountry, merged data set that provides an unprecedented opportunity for cross-national comparison of the patterns, predictors, and consequences of substance use and disorders of substance use. Analyses of existing data from Canada, Mexico, Germany, the Netherlands, and the United States revealed that there is variation across sites in the prevalence of alcohol and drug use, dependence, and associated problems, as well as in the prevalence of specific psychiatric disorders, including mood, anxiety, conduct, and adult antisocial behavior disorders. However, there is strong similarity across sites in the association between certain psychiatric disorders and drug use disorders. For all sites, mood disorders and anxiety disorders were found to be significantly associated with drug use, dependence, and associated problems. Cross-national studies such as this can provide clues to culture-specific risk factors or, if findings are similar across cultures, may suggest that the consistency in results is attributable to some other stable human characteristics that are independent of social and cultural factors.

A supplement awarded in September 1999 to the National Development Research Institute, Inc., New York City, New York, supports a cross-border HIV prevention project for injection drug users and their sexual partners. The project is being conducted in Yunnan Province, China, and Lao Cai, Viet-

nam. The Swedish International Development Agency and the Ford Foundation are also contributing financial support to the project. NIDA supported the design of the HIV prevention intervention and its evaluation in the project's 1st year, in FY 99. Work involves site visits to candidate villages for the intervention and finalization of the intervention and evaluation designs in collaboration with the in-country partners in China and Vietnam. The investigators are working to develop the process of formulating and implementing cross-border and multinational HIV prevention projects and strategies for assisting those seeking to initiate cross-border joint projects. They also plan to build on findings from this effort to expand the project. This study represents an important opportunity for research on coordinated programs that might reduce the spread of HIV across national borders in areas of the world in which the HIV epidemic is rapidly increasing among injection drug users.

## Division of Treatment, Research, and Development

NIDA's Division of Treatment, Research, and Development continues to collaborate with a pharmaceutical company in Bristol, England, on the development of buprenorphine as a treatment medication for opiate dependence. The research is conducted under a Cooperative Research and Development Agreement between NIDA and the company, which has been in place since September 1993. This joint effort resulted in the development of two products. The first is a sublingual tablet containing buprenorphine alone; the second is a sublingual tablet containing buprenorphine combined with naloxone to reduce potential diversion. The company has filed New Drug Applications for both products, and the U.S. Food and Drug Administration has determined that each product is "Approvable." Buprenorphine is approved for the treatment of opiate dependence in 14 countries and is under review in three others. The clinical pharmacology studies and multisite clinical trials supported by NIDA are critical to the successful approval of these medications.

In conjunction with the Fogarty International Center's International Cooperative Biodiversity Group (ICBG) Program, which receives joint funding from the National In-

stitutes of Health (NIH), the National Science Foundation, and the U.S. Department of Agriculture, the NIDA Division of Treatment, Research, and Development supports one of the ICBG grant projects on Drug Development and Conservation of Biodiversity in West Africa. The purposes of the Program are (1) to improve human health through the discovery of new pharmaceutical, crop protection, and veterinary agents to treat diseases of importance in both developed and developing countries; (2) to promote scientific and economic activity in less developed countries by sharing the benefits of the drug discovery and the conservation research process and products; and (3) to conserve biological diversity through understanding and valuation of diverse biological organisms and development of local capacity to manage these natural resources.

The investigator conducts a broad program to screen plant extracts for development of medicines from plants, for activity against viruses, as well as *Leishmania*, *Trypanosoma*, *Trichomonas*, and malaria. NIDA's primary interest in this project is to discover extracts that have activity in the central nervous system. The active compounds of several of these plant extracts have been isolated and identified.

## Activities With International and Multinational Organizations World Health Organization

NIDA serves as a World Health Organization (WHO) Collaborating Center on Drug Dependence. The two major joint efforts are research and information exchange.

A NIDA researcher and a NIDA staff member served as consultants to the WHO Substance Abuse Department (WHO/SAD) on strategies for developing a global drug abuse database. At a meeting in Vancouver, British Columbia, they worked with WHO/SAD staff and consultants from other countries to develop a phased approach to collecting international epidemiologic data. This approach initially would entail solicitation of available data from different nations to produce a report on drug abuse similar to the report on alcohol abuse published previously by WHO/SAD. This new report would be based on collection of data in a manner similar to that for the periodic surveys conducted by the United Nations Drug Control Program. This first phase would be followed

by the identification of countries to serve as models for development of data systems on the epidemiology of drug abuse and by the initiation of mentoring relationships that pair countries having more advanced systems with those needing assistance.

#### **Global Research Network on HIV Prevention in Drug-Using Populations**

NIDA, the NIH's Office of AIDS Research, the Centers for Disease Control and Prevention. Health Canada, the Joint United Nations Program on HIV/AIDS, and WHO/SAD cosponsored and convened the second annual meeting of the Global Research Network on HIV Prevention in Drug-Using Populations, in Atlanta, Georgia, in August 1999. The Network meeting provided for regional updates in the following areas:

- presentation of epidemiologic and ethnographic data about the global nature and identification of emerging issues in the HIV epidemic, including the implications for risk of hepatitis B virus and HCV in drugusing populations;
- discussion on the nature, status, and effectiveness of HIV prevention efforts among injection drug users in different countries:
- planning of approaches to facilitate the use and application of the best science-based practices for HIV prevention; and
- sharing of research ideas, development of protocols, and identification of sources of support for cross-national HIV prevention research, through increased collaborative efforts among national and international researchers.

Network participants also explored the potential for developing linkages with other regional, national, and international networks that focus on HIV interventions among drug users; the translation of findings into best practices to prevent the spread of HIV among drug users; and methods to ensure that recent findings about effective intervention strategies are shared.

### **Extramural Programs**

#### **Grants**

During FY 99, NIDA supported 21 foreign grants and 14 grants with a foreign component. These grants are administered by the Division of Epidemiology, Services, and Prevention Research: the Division of Neuroscience and Behavioral Research: the Division of Treatment, Research, and Development; and the Center on AIDS and Other Medical Consequences of Drug Abuse.

#### **Contracts**

In FY 91, NIDA created the INVEST Program. The goals of the Program are

- 1. to foster collaboration within the international community of scientists engaged in research on drug abuse;
- 2. to expand the international network of drug abuse researchers who are knowledgeable in the areas of science related to NIDA's mission:
- 3. to broaden the dissemination of findings from NIDA's drug abuse research to the international community; and
- 4. to provide scientific and technical consultation on drug abuse research to foreign investigators, ministries of health in other countries, and international organizations.

Activities supported through NIDA's IN-VEST Program expand international scientific knowledge about drug abuse while promoting development of rigorous scientific research. Through the Program, NIDA is building an international network of scientists capable of augmenting the research conducted and supported by the Institute.

#### **International Meetings**

During FY 99, NIDA supported several research workshops and conferences in collaboration with other countries and international organizations.

A seminar to promote cooperation between NIDA and the Spanish National Plan on Drugs was held in Madrid, Spain, in September 1998. The seminar was entitled Evaluating Drug Abuse and Drug Abuse-Related HIV/AIDS Prevention Programs.

The U.S.-Russia Binational Workshop on Drug Abuse and Infectious Disease Prevention Strategies was held in St. Petersburg, in May 1999. NIDA and Pavlov Medical University, St. Petersburg, organized the meeting. Four NIDA staff members, one NIH staff member, and nine NIDA-funded researchers presented plenary speeches and conducted workshops on a variety of prevention-oriented topics. A small assistance program to begin development of prevention projects in Russia was announced. NIDA staff and researchers worked with Russian partners in developing project proposals, which are being reviewed.

The 61st Annual Scientific Meeting of the College on Problems of Drug Dependence, in Acapulco, Mexico, in June 1999, was partially supported by a grant from NIDA.

#### **Interagency Agreements**

Training and Technical Assistance

Meetings of the East and South Asian Multi-City Epidemiology Work Group were held in Penang, Malaysia, in November 1998 and May 1999. The work group is a network for epidemiologic surveillance of drug abuse. It is composed of researchers throughout the Asian region, including Bangladesh, Cambodia, China, India, Japan, Laos, Malaysia, Myanmar, Pakistan, Papua New Guinea, the Philippines, Sri Lanka, Thailand, Vietnam, and Taiwan.

Meetings of the South African Community Epidemiology Network on Drug Use were held in Cape Town, in October 1998, and in Cape Town, Port Elizabeth, Durban, and Johannesburg, in March 1999.

The 3rd meeting of the U.S.-Mexico Border Epidemiology Work Group was held in San Diego, California, in July 1999. This work group is composed of researchers and drug abuse program officials from national offices and from state and sister-city agencies along the border.

#### International Epidemiology Work Group on Drug Abuse

The 6th annual meeting of the International Epidemiology Work Group on Drug Abuse was held jointly with the 46th meeting of NIDA's Community Epidemiology Work Group and the Canadian Community Epidemiology Network on Drug Use, in Vancouver, in June 1999. The work group is a network of members of national and regional epidemiology work groups and international agency officials, who meet to present and discuss the global patterns and trends of drug abuse and emerging problems. Work groups and agencies participating in the meeting included the following:

- NIDA's Community Epidemiology Work Group;
- Australian Epidemiology Work Group on Drug Use;
- Canadian Community Epidemiology Network on Drug Use;
- Mexican Epidemiologic Surveillance System of the Addictions;

- South African Community Epidemiology Network on Drug Use;
- Organization of American States Inter-American Drug Abuse Control Commission;
- East and South Asian Multi-City Epidemiology Work Group;
- European Monitoring Centre on Drugs and Drug Addiction;
- United Nations International Drug Control Program; and
  - WHO/SAD.

#### **Intramural Programs and Activities**

NIDA's Intramural Research Program is located at the Addiction Research Center, Baltimore, Maryland. During FY 99, the Intramural Research Program hosted 23 Visiting Fellows, 7 Guest Researchers, 3 Special Volunteers, 3 Visiting Associates, 2 Visiting Scientists, 1 Courtesy Scientist, and 1 Professional Service Contract. These visitors were from the following countries: Australia, Belarus, Canada, China, Colombia, the

Czech Republic, France, Germany, Israel, Italy, Japan, Jordan, the Philippines, Poland, Russia, Spain, Sweden, the United Kingdom, and Taiwan.

#### **Fellowships**

NIDA supports two international fellowships to offer professional research development opportunities to international scientists: the INVEST Research Fellowship and the Hubert H. Humphrey Drug Abuse Research Fellowship. To support NIDA's vision for cooperation in international research, it is important to develop an international cohort of scientists who are knowledgeable about NIDA's research and are trained in accepted methods and current technology.

#### INVEST Research Fellowship

NIDA's INVEST Research Fellowship enables postdoctoral researchers to work with established scientists engaged in drug abuse research at a U.S. institution. Each non-U.S.

scientist receives research training with a NIDA-funded grantee for 1 year. The FY 99 INVEST Research Fellows were from Australia, Egypt, and Spain.

#### Hubert H. Humphrey Drug Abuse Research Fellowship

In cooperation with the U.S. Information Agency and Johns Hopkins University, Baltimore, NIDA sponsors a unique component of the Hubert H. Humphrey Drug Abuse Research Fellowship Program. This fellowship is designed to provide midcareer professionals in the field of drug abuse from developing countries with exposure to state-of-the-science methods and research advances. The Program also provides the basis for establishment of research linkages leading to future international research.

The Hubert H. Humphrey Drug Abuse Research Fellows funded by NIDA in FY 99 were from India, Romania, South Africa, and Ukraine.